

REMARKS

I. Status of the Claims

Claims 1-25 were originally filed. As the result of a restriction requirement, claims 13-25 have been withdrawn. Upon entry of the present amendment, claim 6 and all withdrawn claims are canceled. Claims 1-5 and 7-12 remain pending. Claim 1 is amended to import the limitation of claim 6 as originally filed. Claims 7-12 are amended to delete the word "derived" and to modify dependency to reflect the deletion of claim 6. No new matter is introduced.

II. Claim Rejections

A. 35 U.S.C. §112, Second Paragraph

Claims 6-12 were rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Specifically, the Examiner stated that "derived" makes it unclear whether any or what changes may be involved during the "derivation" process. As amended, the word "derived" is deleted from all relevant claims, which renders the indefiniteness rejection moot. Applicant wishes to thank the Examiner for her helpful suggestion regarding this particular claim amendment.

B. 35 U.S.C. §102

Gilbert

Claims 1-3 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Gilbert *et al.* Applicant respectfully traverses the rejection, particularly in light of the present amendment.

To anticipate a pending claim, a prior art reference must provide, either expressly or implicitly, each and every limitation of the pending claim. MPEP §2131. As amended, claims 1-3 are directed to a composition comprising a serum in which a plurality of heterologous antibodies are dissolved. These antibodies are independently IgG or IgM, and each of them specifically binds to a different antigen. These antigens are from one or more organisms independently selected from the group consisting of *Toxoplasma gondii*, Rubella virus,

Cytomegalovirus (CMV), Herpes Simplex Virus type-1 (HSV-1), Herpes Simplex Virus type-2 (HSV-2), Mumps Virus, Measles Virus, Epstein-Barr Virus (EBV), Varicella Zoster Virus, *Borrelia burgdorferi*, *Treponema pallidum*, *Helicobacter pylori*, and *Mycoplasma pneumoniae*.

In contrast, the Gilbert reference relates to the presence of naturally occurring antibodies against nine common antigens in human sera, such as actin, tubulin, and collagen. The reference does not discuss antibodies against antigens from any of the organisms named above. Thus, the Gilbert reference does not provide or suggest all limitations of the pending claims and cannot anticipate the claims. Applicant therefore respectfully requests that this anticipation rejection be properly withdrawn.

Berneman

Claims 1-5 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Berneman *et al.* Applicant respectfully traverses the rejection, particularly in light of the present amendment.

As discussed above, a reference must provide all limitations of a claim in order to anticipate the claim. The amended claim 1 recite a plurality of heterologous antibodies having specificity for different antigens selected from a list of specific organisms; the Berneman reference, on the other hand, relates to antibodies against self antigens found in mouse serum. No antibody with specificity for antigens from any organisms within the list of claim 1 is mentioned or suggested in this paper. Thus, the Berneman reference does not anticipate the currently pending claims. The withdrawal of the anticipation rejection based on this reference is respectfully requested.

Luka

Claims 1-3 and 6-8 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Luka *et al.* Applicant respectfully traverses the rejection.

The pending claims are directed to a composition comprising a serum in which a plurality of heterologous antibodies are dissolved. The Luka reference describes a new ELISA method for detecting antibodies against EBV antigens in serum samples. The serum samples

tested in this reference, however, were obtained from individual patients and tested separately, since there was no "pooling" of the individual sera prior to ELISA. In other words, these serum samples do not constitute a composition comprising heterologous antibodies, which are defined in the specification as antibodies not naturally present in the same source (paragraph 32 on page 7).

Further, the experiments in Luka *et al.* show a correlation in the results between the new ELISA method and an immunofluorescence (IF) test for detecting different EBV antigens, such as VCA, EA, EBNA, and MA. Yet, the description and results in the reference indicate that the ELISA and IF assays for each of these EBV antigens were performed separately with individual sera. The reference therefore does not provide unequivocal evidence that any one given serum contains a plurality of antibodies with specificity against different EBV antigens.

As such, the Luka *et al.* reference does not provide or suggest all limitations of the pending claims and is therefore not an anticipatory publication. The withdrawal of the anticipation rejection based on this reference is respectfully requested.

Wong

Claims 1 and 6 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Wong *et al.* Applicant respectfully traverses the rejection.

The Wong reference describes a calibrator that contains a composite antibody, which is a non-specific IgM covalently conjugated to a non-IgM that is specifically reactive to an infective organism, such as toxoplasma, rubella, cytomegalovirus, and herpes. This composite antibody essentially provides a modified antibody that has both a desired binding specificity for an antigen of interest, which is provided by the non-IgM antibody, and a universal IgM Fc segment, which is provided by the non-specific IgM and acts as a detectable moiety in a diagnostic assay because the Fc portion of the non-specific IgM can be recognized by a secondary anti-IgM antibody. Thus, this composite antibody described by Wong *et al.* has only one antigen binding specificity. This is further evidenced by the description in, *e.g.*, column 3,

lines 20-23, where the non-specific IgM in the composite antibody is said to be either a whole antibody or just the Fc portion, which does not include the antigen-binding variable domain of an antibody.

Claim 1 of this application is directed to a composition comprising a serum in which a plurality of heterologous antibodies (IgM or IgG) are dissolved. The claim language requires that each of the antibodies specifically binds to different antigens originated from a list of specified organisms. The Wong reference does not provide this limitation, because, as stated above, one of the conjugation partners, the non-specific IgM, is by definition an antibody that does not specifically bind to any particular antigen of interest (such as one from an infectious organism). In some cases, the non-specific IgM consists of only the Fc portion and does not even have the variable domain necessary for antigen-binding.

Although it is stated in the Wong reference (*e.g.*, column 2, lines 37-44; column 5, lines 17-21) that the calibrator can be used for testing antibodies against multiple infectious pathogens, a review of the reference in the entirety indicates that this statement refers to the use of several different calibrators of this kind, instead of one single calibrator.

As such, it is not established that the Wong reference teaches or suggests all the limitations of claim 1. Applicant therefore respectfully request that the Examiner withdraw the anticipation rejection based on Wong *et al.*

C. 35 U.S.C. §103

Wong in view of Desmonts

Claim 10 was rejected under 35 U.S.C. §103(a) for alleged obviousness over Wong *et al.* in view of Desmonts *et al.* Applicant respectfully traverses the rejection.

In order to establish a *prima facie* showing of obviousness, three requirements must be satisfied: all limitations of a pending claim must be expressly or impliedly disclosed by prior art references; there must be a suggestion or motivation in the art for one skilled artisan to combine the limitations; and there must be a reasonable expectation of success in making such a combination. MPEP §2143.

As stated above, the currently pending claim 1 is drawn to a composition comprising a serum in which a plurality of heterologous antibodies are dissolved. These antibodies are independently IgG or IgM, and each of them specifically binds to a different antigen. These antigens are from one or more organisms independently selected from the group consisting of *Toxoplasma gondii*, Rubella virus, Cytomegalovirus (CMV), Herpes Simplex Virus type-1 (HSV-1), Herpes Simplex Virus type-2 (HSV-2), Mumps Virus, Measles Virus, Epstein-Barr Virus (EBV), Varicella Zoster Virus, *Borrelia burgdorferi*, *Treponema pallidum*, *Helicobacter pylori*, and *Mycoplasma pneumoniae*. Also as discussed above, the Wong *et al.* references does not provide or suggest all limitations of claim 1, namely the limitation of a calibrator containing multiple antibodies that specifically binds to different antigens derived from infectious pathogens.

The Desmonts reference teaches an assay system for detecting IgG and IgM specifically reactive to *T. gondii*. Yet, this references does not supply the missing limitation of a calibrator containing multiple antibodies specifically reactive to different antigens. Therefore, the Wong and Desmonts references fail to provide all limitations of claim 10, which depends from claim 1. The withdrawal of the obviousness rejection is respectfully requested.

Wong in view of Desmonts, Gans, Yi, Krell, and Luka

Claims 9 and 11 were rejected under 35 U.S.C. §103(a) for alleged obviousness over Wong *et al.* in view of Desmonts *et al.*, Gans *et al.*, Yi *et al.*, Krell *et al.*, and Luka *et al.* Applicant respectfully traverses the rejection.

Claims 9 and 11 both depend from claim 1. As indicated by the above discussion, the limitation of a calibrator containing multiple antibodies that specifically binds to different antigens derived from infectious pathogens is not provided or suggested by Wong *et al.* and Desmonts *et al.*. None of the Gans, Yi, Krell, and Luka references supply this limitation either, as Gans, Yi, and Krell each describes detection of antibodies against certain organisms, and Luka describes a new ELISA method. Because not all claim limitations are provided by these references, Applicant submits that no *prima facie* obviousness has been established. The withdrawal of this rejection is thus respectfully requested.

Wong in view of Desmonts, Gans, Yi, Krell, Luka, and Lo

Claim 12 was rejected under 35 U.S.C. §103(a) for alleged obviousness over Wong *et al.* in view of Desmonts *et al.*, Gans *et al.*, Yi *et al.*, Krell *et al.*, Luka *et al.*, and Lo *et al.* Applicant respectfully traverses the rejection.

Claim 12 depends from claim 1. Similar to the discussions in the previous section, the references by Wong *et al.*, Desmonts *et al.*, Gans *et al.*, Yi *et al.*, Krell *et al.*, and Luka *et al.* fail to provide the limitation of a calibrator containing multiple antibodies that specifically bind to different antigens from infectious organisms; the Lo reference, on the other hand, merely adds the description on detection of *M. pneumoniae* antibody. Thus, when viewed together, these cited references fail to provide all limitations of claim 12 and hence cannot render claim 12 obvious. The withdrawal of the rejection on this ground is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Chuan Gao
Reg. No. 54,111

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
CG:cg
60468480 v1